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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/776,044	02/26/1997	MARGARET BYWATER	1614-178P	1463

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/776,044	Applicant(s) BYWATER ET AL.	
	Examiner MISOOK YU, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 14 and 15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 14 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed on 12/05/2003 is acknowledged. Claim 3 is amended. Claims 1-10, 14, and 15 are pending, and are under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

At the first page under REMARKS, applicant requests an interview. Applicant is kindly requested to call the examiner in charge of the application (the telephone number is listed at the second last page of this Office action) at least a week ahead of the desired interview date to schedule an interview.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 3 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

Claim 15 remain rejected for reason of record under 35 U.S.C. 102(e) as being anticipated by Vogelstein et al (US PAT 5,527,676; issued June 18, 1996; effective filing date of December 6, 1989).

Applicant argues that Vogelstein et al fail to disclose a method for prognostication of the development of neoplasia in a human patient because Vogelstein et al discloses the sequencing of entire coding region of p53, not just exons 2-11 of p53. This argument has been fully considered but found not persuasive because exons 2-11 of p53 is within the entire p53, therefore disclosing the entire p53, Vogelstein et al

discloses exons 2-11 of p53. Applicant further argues that Vogelstein et al fails to associate the metastatic potential of the neoplasia based on the presence, position, and type of mutation, nor does Vogelstein et al suggests that certain mutations in p53 are indicative of poor patient outcome. These arguments are considered as arguing limitations not presented in the claim because the claim is drawn to determine whether presence or absence of mutation, and determine prognosis based on presence of absence of a mutation. Note claim construction, especially b) and d). The active steps of the claim does not say anything about certain mutations in p53, and/or position, and type of mutation in p53.

As stated before in the previous Office action, Vogelstein et al teach at column 1 (see also page 7 Paragraph # 13 of the prior Office action, Paper No. 25) that the reason for undertaking the study disclosed in the patent is to define the particular genetic region in the short arm of chromosome 17 responsible for progression of curable adenoma to lethal carcinoma. Vogelstein et al teach that that specific genetic region is the gene encoding p53 and mutation in that specific genetic region is responsible for progression of benign, curable disease to lethal carcinoma (indicative of poor patient survival), thus Vogelstein et al teach a method of prognostication of the development of neoplasia by detecting a mutation in p53. The broadly written claim 15 thus reads on the prior art.

Claim Rejections - 35 USC § 103

Claims 1, 2, 4-10, and 14 remain rejected for reason of record under 35 U.S.C. 103(a) as being unpatentable over Vogelstein et al as applied to claim 15 above,

and in view of Elledge et al (Breast Cancer Res. Treat. 27, 95-102, 1993), and of Callahan (J. Natl. Cancer Institute, 83, 826-7, 1992) and further in view of Hedrum (IDS, BioTechniques, 17, 118-29, 1993).

Applicant appears to argue that since the primary reference (Vogelstein et al) used in 102 rejection above does not teach the invention, this rejection should also fall. However, the 102 rejection still stands for the reasons given above. Applicant does not argue the the secondary references or the tertiary reference.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

Applicant states (at the first paragraph of page 8 of the amendment filed on 12/05/2003) that the specification teaches: at page 3 lines 9-19, that 70 % of p53 mutations are missense mutations change the identity of an amino acid and alter the confirmation and stability of p53; at page 7 line 32-38, that p53 mutation causing truncation of p53 protein is detrimental because the truncated protein could not do its work (i.e. DNA proof-reading); at page 8 lines 3-10, that p53 mutation(s) detrimental to patient are those that affect the DNA binding or transactivation, whareas those

mutations less harmful for a patient are amino acid substitution mutations (i.e. missense) that do not greatly affect structure or function of P53.

The specification as originally filed teaches that: at page 3 lines 9-19, that most (70 %) of p53 mutations are missense; at page 7 line 32-38, that a p53 nonsense mutation that puts a transcriptional stop, which will result in a truncated p53 protein is detrimental; at page 8 lines 3-10, that analysing any encoding region of p53 DNA (i.e., all or part of exons) will reveal what mutation(s) is detrimental to patient since such mutation will result in loss of p53 wild-type functions. Thus, the specification as originally filed teaches a nonsense or frameshift mutation close to N-terminal end of p53 is more harmful than a nonsense or frameshift mutation near the C-terminal end. In other words, specification as originally filed teaches that a nonsense mutation in "conserved region III" is indicative of worse outcome than a frameshift or nonsense mutation in the "conserved region V" because "conserved region III" is close to the N-terminal than "conserved region V". In summary, the specification as originally filed does not teach the newly recited limitations in the specific conserved regions are associated with the outcome. Applicant is kindly requested to point out the support in the specification as originally filed since it is not apparent to the Office.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 08/776,044
Art Unit: 1642

Page 7

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

A handwritten signature in black ink, appearing to be 'L. Helms', written in a cursive style.

LARRY R. HELMS, PH.D.
PRIMARY EXAMINER

LARRY R. HELMS, PH.D.
PRIMARY EXAMINER